

Neuromyelitis optica antibody (NMO-IgG) status in Indian patients with multiple sclerosis and allied demyelinating disorders

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Abstract

Clinical studies in India have consistently reported high incidence of optic nerve and spinal cord involvement in patients diagnosed to have multiple sclerosis (MS). Though speculated, it is not clear whether the neuromyelitis optica (NMO) spectrum of disorders are responsible for this site specificity. Seventy eight patients with clinical and magnetic resonance imaging features consistent with demyelinating disorders were evaluated for the presence of serum NMO-IgG (anti-AQP4 antibody). Of the patients, 54 (69%) patients belonged to the NMO spectrum disorders. NMO-IgG was positive in 3 female patients - one each of optic-spinal MS, NMO and recurrent acute transverse myelitis. In this small Indian series of MS and allied demyelinating disorders, NMO-IgG seropositivity was low.

INTRODUCTION

Optic-spinal phenotype of multiple sclerosis (MS) dominates demyelinating disorders in Asia, among Japanese¹ as well as Indian patients², with Asian MS becoming synonymous with the Japanese optic-spinal MS. It has been suggested that neuromyelitis optica (NMO) is a disease entity distinct from MS.³ This is said to be supported by high prevalence of anti-AQP4 antibody (NMO-IgG) found among NMO patients.⁴ It has also been reported that optic-spinal MS among Japanese has high positivity of NMO-IgG, thus it may be the same disease as NMO reported in the West.⁵

The common occurrence of spinal cord and optic nerve involvement in Indian patients with MS has been consistently reported in several hospital based studies since the 1950's.^{2,6} It has been speculated that this may be due to over representation of NMO and its variants among the Indian patients with demyelinating disorders.⁷ As NMO-IgG is 91% specific and 100% sensitive⁸ in NMO, a reliable tool to distinguish NMO spectrum of disorders from other demyelinating illnesses, we therefore undertake to determine the status of the antibody in our patients with MS. This include conventional MS, optic-spinal MS, as well as disorders which clinically and radiologically resembled NMO; acute transverse myelitis (ATM), recurrent ATM, and recurrent optic neuritis, to evaluate the role of NMO among our patients with demyelinating disorders.

METHODS

A total of 78 patients (46 males and 32 females) were enrolled in this study. These consisted of conventional MS (16), optic-spinal MS (14), NMO (8), ATM (26), recurrent ATM (6), and recurrent optic neuritis (8). Clinical and demographic details, and results of investigations were collected and compiled in all patients. Sera were collected for NMO-IgG estimation during the acute phase of illness and transported to Neuroimmunology laboratory, Mayo Clinic, Rochester, Minnesota, USA for testing.

Diagnostic criteria

All patients diagnosed to have MS fulfilled McDonald criteria.⁹ Optic-spinal MS was defined as relapsing remitting MS with clinical attacks confined to the spinal cord (acute partial transverse myelitis) and optic nerve. Acute partial transverse myelitis was defined as patients exhibiting mild symmetrical sensory and/or motor symptoms or marked asymmetrical motor and/or sensory symptoms.¹⁰ All NMO patients satisfied criteria of Wingerchuck et al.¹¹ ATM was defined as complete spinal cord dysfunction with a sensory level and bladder dysfunction and supported by linear spinal cord lesions on MRI extending more than 3 vertebral segments. When such events recurred, the term recurrent ATM was used. Long cord lesion was defined as spinal MRI lesions extending more than three vertebral segments.

RESULTS

Clinical and radiological profile of the study patients

The details of the study patients are shown in Table 1.

MS patients

Among the 30 patients diagnosed to have MS, 16 patients had clinical and radiological feature consistent with conventional MS. There was female predominance (80%) and mean age of onset of disease was 25 ± 2 years. Oligoclonal bands were present in CSF in 50% of patients. Among the optic-spinal MS patients, mean age of onset was 38 ± 17 years. Two patients had longitudinal spinal cord lesions exceeding 3 vertebral segments but MRI brain was indistinguishable from conventional MS. One of the optic-spinal MS patients had NMO-IgG.

NMO spectrum disorders

Five patients fulfilled the Wingerchuck diagnostic criteria of 1999.¹² In addition there were 3 patients who had large brain lesions during the course of their illness. The first patient was a 24 year-old male, who had 5 relapses over a period of 10 years. These included four relapses of ATM and one optic neuritis. During his third relapse he developed quadriplegia requiring ventilatory

support. In his most recent relapse he developed dysarthria, headache and disorientation. His spinal MRI showed long cord lesion extending 9 vertebral segments. His brain MRI in the last relapse showed a tumefactive brain lesion. He received steroids during each relapse and remained independent with minimal visual disability (VA 0.67) and EDSS score of 2. The second patient was a female with onset of illness at 49 years. She had 4 relapses, 2 each of ATM and optic neuritis over 8 years. Her brain MRI showed 2 large lesions in the subcortical white matter. MRI of the dorsal cord showed long cord lesion extending to 5 vertebral segments. She has moderate visual disability (VA – 0.33 in worse eye), and an EDSS score of 3.5. The third patient was a male. At the age of 50 years, he had first attack of ATM. This was followed over a 4-year period by two more attacks of ATM and one attack of optic neuritis. During his fourth relapse, he develop dysarthria and had gaze dependent nystagmus in addition to ATM. Brain MRI showed two lesions in brainstem and left cerebellar hemisphere. Currently he has VA of 0.33 and EDSS score of 2.5. There were 6 patients with recurrent ATM. One patient had a large cerebellar lesion and another had 2 large subcortical lesions during the course of illness. There were 8 patients with recurrent optic neuritis. Five patients had relapses at least once unilaterally, and 3 patients relapsed bilaterally. Their VA ranged from 0.34 – 0.67.

Table 1: Clinical, laboratory and MRI features of patients tested for NMO-IgG

	MS		NMO	ATM	Recurrent ATM
	Optic-spinal	Conventional			
Number	14	16	8	26	6
Male/ female	6/8	6/10	5/3	17/9	4/2
Age at onset (SD)	38 (17)	25 (2)	40 (10)	38 (10)	42 (11)
Duration of disease (SD)	5 (2)	4 (2)	7 (3)	NA	5 (2)
EDSS (median)	2.5 (2-6.5)	2 (1-3.5)	2.5 (1.5-6)	2 (1-3.5)	3.5 (3-7)
Cerebrospinal fluid cell count > 50 /ul	2 (14%)	Nil	6 (75%)	15 (57.6%)	4 (66.6%)
Oligoclonal band	4 (29%)	8 (50%)	Nil	Nil	Nil
MRI					
Long cord lesions*	2 (14%)	Nil	8 (100%)	21 (80.7%)	6 (100%)
Large brain lesions (>1cm)	1(14%)	Nil	3 (37.5%)	Nil	2 (33%)

*Long cord lesions : Lesions longer than 3 vertebral segments in spinal MRI
MS : multiple sclerosis, NMO : neuromyelitis optica, ATM : acute transverse myelitis

Clinical and radiological profile of NMO-IgG positive patients

Three female patients were tested positive for NMO-IgG. They included one patient each of optic-spinal MS, NMO and recurrent ATM. The first patient with optic-spinal MS was a 47 year old female who had recurrent acute partial myelitis interspersed with optic neuritis. Although her spinal cord dysfunction improved with steroids initially, her visual disability steadily increased. At the end of 4 years, her left eye had only light perception and right eye visual acuity (VA) was 0.3. During her last documented relapse, she developed quadriparesis from which she never improved (EDSS 6.5). MRI brain was consistent with the diagnosis of MS. MRI of the spinal cord showed long cord lesion extending over 5 vertebral segments. The second patient with NMO was 38 years old at the onset of disease. She had three relapses, two of ATM and one of optic neuritis, during a 3 year period and has a current EDSS score of 5.5. Her brain MRI was normal. The third patient with recurrent ATM was 42 years old. She developed 2 episodes of ATM at 7 months interval. She had long cord lesion in the cervical region during her first attack and required ventilatory assistance. MRI brain was normal. Her EDSS score at follow up was 4.

DISCUSSIONS

The clinical and radiological profile of our patients was largely similar to reports from other parts Asia. Atypical features seen in our patients were male predominance especially in the NMO and ATM group of patients. Several Indian studies have reported a male predominance among patients with MS.^{2,13} A bias in hospital admissions in favor of male patients cannot be ruled out, especially since supportive data from community based data on MS is not available from India.

Another atypical feature seen in our patients was the good clinical outcome for patients with recurrent long cord lesion in spite of long duration of illness. These patients with good outcome have clinical features consistent with NMO spectrum disorders. There were similar reports of favorable outcome from other centers in India. Pradhan et al¹⁴ described 6 patients (3 male and 3 female) with clinical and radiological features consistent with relapsing NMO who recovered well after recurrent attacks of visual loss and myelitis, remaining ambulant 2-10 years after onset of disease. Three of our patients with NMO and 2 with recurrent ATM had large brain lesions during the course of

their disease. This is not unusual as large lesions, and even tumefactive lesions have been described occasionally in patients with NMO.¹⁵

In this small study from southern India, only 3/78 (4 %) patients were tested positive for NMO-IgG. Out of 78 patients tested, with the exception of the 16 conventional MS patients, all others were consistent clinically with NMO spectrum disorders. Yet NMO-IgG seropositivity in these Indian patients was low. The common occurrence of spinal cord and optic nerve involvement in Indian patients with MS and allied demyelinating disorders is thus not explained by over representation of NMO and NMO spectrum disorders among the Indian patients.

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